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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,139	01/10/2006	Herve Rolland	SERVIER 479 PCT	6115

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EXAMINER	
RICCI, CRAIG D	

ART UNIT	PAPER NUMBER
4161	

MAIL DATE	DELIVERY MODE
07/14/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/564,139	ROLLAND ET AL.	
	Examiner	Art Unit	
	CRAIG RICCI	4161	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *1/10/2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *7-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/13/2006 and 1/10/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 7-12 are currently pending and the subject of this Office Action. Claims 1-6 are cancelled. This is the first Office Action on the merits of the claims.

Information Disclosure Statement

2. The information disclosure statement filed 1/10/2006 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Priority

3. The earliest effective filing date afforded the instantly claimed invention has been determined to be 07/16/2004 as to claims 7-12.

4. Acknowledgment is made of Applicant's claim for foreign priority pursuant to 35 U.S.C. 119(a) and 365(b) based on a prior application filed in France on 07/17/2003. The certified copy has been filed in parent Application No. PCT/FR04/01867, filed on 07/16/2004.

Specification

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use:

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.

(b) CROSS-REFERENCE TO RELATED APPLICATIONS.

(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.

(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.

(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.

(f) BACKGROUND OF THE INVENTION.

(1) Field of the Invention.

(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.

(g) BRIEF SUMMARY OF THE INVENTION.

(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).

(i) DETAILED DESCRIPTION OF THE INVENTION.

(j) CLAIM OR CLAIMS (commencing on a separate sheet).

(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).

(l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. **Claim 7 rejected under 35 U.S.C. 102(a) and 102(e) as being anticipated by *Quay* (US 2004/0028613 A1) filed June 25, 2001**.

6. Instant claim 7 is drawn to a pharmaceutical composition in the form of an aqueous solution or powder for nasal administration of piribedil, comprising piribedil, optionally a cyclodextrin, and one or more pharmaceutically acceptable excipients. *Quay* teaches "compositions for mucosal delivery of dopamine receptor agonists" (Paragraph 0046), specifically **piribedil** (Paragraph 0048) and "mucosal delivery-enhancing agents" specifically "a **cyclodextrin** or beta-cyclodextrin derivative" (Paragraph 0038) and **excipients** (Paragraph 0053) in the form of "an **aqueous**

solution, e.g., as a **nasal spray**" (Paragraph 0453) or "dry **powder** formulations" (Paragraph 0455). Accordingly, *Quay* anticipates each of the elements of instant claim

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. **Claims 7-12 rejected under 35 U.S.C. 103(a) as being unpatentable over *Merkus* (US 5,756,483) in view of *Deleu et al* (Clin Pharmacokinet 41(4):261-309, 2002)**.

10. As discussed above, instant claim 7 is drawn to a pharmaceutical composition in the form of an aqueous solution or powder for nasal administration of piribedil, comprising piribedil, optionally a cyclodextrin, and one or more pharmaceutically acceptable excipients. More specifically, the piribedil is in the form of the base (claim 8) and the cyclodextrin is a partially methylated β-cyclodextrin (claim 9) wherein the degree of substitution by methyl groups is about 1.7 (claim 10). *Merkus* teaches

pharmaceutical compositions for intranasal administration of apomorphine, a "very potent dopamine agonist... used as an adjunctive medication in the treatment of Parkinson's disease" (Column 3, Lines 53-56). More specifically, *Merkus* teaches apomorphine in the form of the base (Column 5, Example 1A, Line 28) and *Merkus* also teaches apomorphine in combination with a cyclodextrin, preferably "methylated β-cyclodextrin with a degree of CH_3-substitution between 0.5 and 3.0, more preferably between 1.7 and 2.1" (Column 4, Lines 26-31). Additionally, *Merkus* teaches that "many other excipients, known in the pharmaceutical literature, can be added" to the disclosed composition (Column 5, Lines 7-9) and the composition can be administered "as a nasal spray... or powder" (Column 4, Lines 36-38). However, *Merkus* does not teach piribedil. Thus, although *Merkus* teaches each of the elements of instant claims 7-10, *Merkus* does not teach a composition comprising piribedil. Rather, the composition that *Merkus* teaches comprises apomorphine. Accordingly, the only difference between claims 7-10 of the instant application and *Merkus* is that Applicant has replaced apomorphine in the composition taught by *Merkus* with pirebedil.

11. *Deleu et al* teaches that apomorphine and piribedil are both dopamine agonists with similar mechanisms of action, similar effects and similar uses such as the treatment of Parkinson's disease (entire document). In the case of Parkinson's disease, *Deleu et al* specifically teach that "no single best treatment exists for an individual patient with Parkinson's disease. Particularly in the advanced stage of the disease, treatment should be individually tailored" (abstract).

12. It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to replace apomorphine with piribedil in the composition taught by *Merkus*. Accordingly, one of ordinary skill in the art would have been motivated to use, in place of apomorphine in the invention taught by *Merkus* useful in the treatment of Parkinson's disease, other dopamine agonists useful in the treatment of Parkinson's disease, such as piribedil. Since it would have been obvious to substitute apomorphine with piribedil in view of *Deleu et al*, and since *Merkus* teaches all the other limitations of instant claims 7-10 as discussed above, claims 7-10 are obvious.

13. Instant claim 11 is drawn to the composition of claim 7 wherein "for a final aqueous solution of 10 ml, the amount of piribedil is from 10 to 500 mg for an amount of cyclodextrin of from 75 to 3750 mg" (claim 11). As drafted, claim 11 defines the amount of piribedil and cyclodextrin as percent weight per volume, and an aqueous solution of 10 ml is not read as limiting. Thus, claim 11 defines a solution wherein the amount of piribedil is from 0.1 to 5% w/v for an amount of cyclodextrin of from 0.75 to 37.5% w/v. *Merkus* teaches a composition wherein the amount of apomorphine is 1% w/v and cyclodextrin is 4% w/v (Column 5, Example 3, Lines 65-67). Alternatively, claim 11 can be read to define the amount of piribedil and cyclodextrin as a ratio of each other, and an aqueous solution of 10 ml is not read as limiting. In this case, claim 11 defines a solution wherein the ratio of piribedil to cyclodextrin is from 1:0.15 to 1:375. The ratio of piribedil to cyclodextrin taught by *Merkus* is 1:4 (Column 5, Example 3, Lines 65-67). As stated in MPEP 2131.03, a specific example in the prior art which is within a claimed

range anticipates the range. Since it would have been obvious to substitute apomorphine with piribedil in view of *Deleu et al* as discussed above, and since *Merkus* anticipates the range of instant claim 11, claim 11 is obvious.

14. Instant claim 12 is drawn to the composition of claim 7 wherein "the composition is in powder form and amount of pirbedil is from 0.1 mg to 20 mg for an amount of cyclodextrin of from 7.5 to 75 mg" (claim 12). As drafted, claim 12 is read to define the amount of piribedil and cyclodextrin as a ratio of each other and the absolute values are not a limitation. Thus, claim 12 defines a composition wherein the ratio of piribedil to cyclodextrin is from 1:0.375 to 1:750. As taught by *Merkus*, for a 10 mg powder formulation, the amount of apomorphine is 1 mg and the amount of cyclodextrin is 5 mg (Column 5, Example 1A, lines 27-31). Accordingly, *Merkus* teaches a composition wherein the ratio of piribedil to cyclodextrin is 1:5 (Column 5, Example 1A, lines 27-31). As stated in MPEP 2131.03, a specific example in the prior art which is within a claimed range anticipates the range. Since it would have been obvious to substitute apomorphine with piribedil in view of *Deleu et al* as discussed above, and since *Merkus* anticipates the range of instant claim 12, claim 12 is obvious. However, assuming arguendo that the absolute values recited by instant claim 12 are limiting, claim 12 is still obvious under *Merkus* in view of *Deleu et al*. As taught by *Merkus*, for a 10 mg powder formulation, the amount of apomorphine is 1 mg and the amount of cyclodextrin is 5 mg (Column 5, Example 1A, lines 27-31). Moreover, *Merkus* specifically teach that "the amount of a powder nasal formulation is generally between 1 and 15 mg" (Column 5, Lines 16-17). Thus, based on Example 1A (Column 5, lines 27-31), a person of

ordinary skill in the art would immediately envisage a 15 mg formulation wherein the amount of apomorphine is 1.5 mg and the amount of cyclodextrin is 7.5 mg.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CRAIG RICCI whose telephone number is (571)270-5864. The examiner can normally be reached on Monday through Thursday, and every other Friday, 7:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Patrick Nolan can be reached on (571) 272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/CRAIG RICCI/
Examiner, Art Unit 4161

/Patrick J. Nolan/
Supervisory Patent Examiner, Art Unit 4161